Medical Treatment of Urinary Tract Infection

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INFECTIONS of the urinary tract can be and should be treated by the physician in general practice or by the internist so long as there are no complications. It is only when such complications exist or arise that the cooperation of the urologist must be sought. This communication is to outline some of the principles of medical regimens and their limitations, as regards infections of the bladder, ureters and kidneys, excluding venereal disease and tuberculosis.

Careful diagnosis is the first prerequisite of good treatment. Pyuria in the male can be due to urethritis and prostatitis. Therefore, the patient should void into two containers, the urine of the second voiding being examined microscopically. Pus or bacteria in this specimen usually comes from the bladder, ureters or kidneys. Pyuria in the female in a voided specimen obviously may be due to genital contamination. The urine should be obtained as a "tube specimen" after careful cleansing of the vulva and the urethral meatus, or the patient should be catheterized.

Prior to the advent, about 15 years ago, of effective and specific chemotherapeutic agents, accurate bacteriological diagnosis was not as important as it is today. At present, to treat a patient with pyelonephritis with, say, a sulfonamide without knowing the organism involved is just as poor practice as is treating a patient with pneumonia without seeking the responsible organism. Such practice may deprive the patient of his only chance to have a correct dianosis made and to be given the best known means of treatment. Moreover, many patients have mixed infections, making accurate bacteriological diagnosis more than ever necessary.

A smear of centrifuged fresh urine stained with Gram solution always should be made, and in many cases a culture taken too. In the male a second voiding is adequate for smear, and even for culture provided the head of the penis and prepuce have been previously cleansed, and provided also the container is sterile. In the female a tube specimen may be used for smear, but urine for culture must be obtained by catheterization.

Acute pyelitis and pyelonephritis (the former probably does not exist without the latter) is an acute febrile illness often with considerable toxicity. In treatment the need for adequate fluids is paramount, and where the oral route is not possible because of vomiting, intravenous infusions are important. A word of caution is not out of place here, for one occasionally sees disregard for the speed of injection, and sees saline given to the point of anasarca. Provided two to three hours is taken per litre of fluid, and not more than two litres of fluid contain saline as well as dextrose, even older debilitated individuals can tolerate such treatment without developing heart failure or edema. Rarely is more than four litres per day necessary or wise.

In addition to fluids these patients are in need of rest and warmth. Their kidney pelves and surrounding parenchymae are edematous and inflamed. The possibility of further irritation of these tissues must be considered when nephrotoxic drugs are administered. Merely alkalinization with potassium citrate or sodium bicarbonate may be wiser for the first few days.

When the acute infection is limited to the bladder there is less danger of further tissue irritation by too early administration of chemotherapeutic agents. Fluids are, of course, important here also. Further added comfort can be given the patient by hot Sitz baths, and, in women, by hot vaginal douches. Symptoms of strangury sometimes respond to alkalinization or to hyoscyamus or to belladonna.

In chronic pyelonephritis and in chronic cystitis many of the same therapeutic principles apply. It is important here to realize that the reason for the chronicity is usually a mechanical difficulty. Some of these mechanical factors will be mentioned later. Treatment of them, of course, falls within the realm of the urological specialist.

The possibility of urinary tract tuberculosis always must be kept in mind when the cause is not apparent. Moreover, tuberculosis can co-exist with other bacterial infections. The diagnosis is made by finding the organism in catheterized urine specimens, or better by culture or by guinea pig inoculation. Except for possible palliation with streptomycin, the treatment is surgical.

The rare fungus and protozoan infections are beyond the scope of this presentation.

SULFONAMIDES

Sulfonamide preparations are discussed first, not because they are the drugs of choice, but because they are used so universally and so rashly not only for urinary tract infections but elsewhere, some of the dangers should be re-emphasized. Fatalities from tubular obstruction are well known, but deaths also have occurred from renal damage and anuria even in the absence of crystalline deposits. Bone marrow depression and death after as many as five weeks with as small a dose as 1 gm. a day have been reported. Followers of Arnold Rich worry about generalized blood vessel sensitization. Such speculation merely enhances the need for caution in the use of a valuable therapeutic agent, and makes it necessary to weigh the possible benefits against the in-

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herent dangers. If another drug offers equal therapeutic promise, that drug should be preferred to sulfonamide. Moreover, sulfonamide should not be administered in the presence of an elevated blood urea. It should not be administered unless the patient is warned to report decrease in urinary output. Blood counts (white cell count and hemoglobin are adequate) as well as urine examination must be done twice a week for at least the first two weeks, and once a week for six weeks during treatment with small doses, more often still with large doses.

Of the sulfonamides, sulfadiazine and perhaps sulfacetimide are probably best. More recently a combination of sulfathiazole and sulfadiazine has shown promise. In severe infections 1 gm. every four hours day and night is usually adequate, in the less severe 0.5 to 1 gm. four times daily. Fluid intake to secure 1000 to 1500 cc. output of urine daily is essential. Added sodium bicarbonate sufficient to alkalinize the urine is desirable. Sulfonamides are useful against bacillus coli, aerobacter aerogenes, staphylococcus and streptococcus. They have no effect against streptococcus fecalis, and rarely against bacillus proteus or pyocyaneus.

PENICILLIN

As the majority of urinary tract infections are caused by Gram-negative bacilli, penicillin has a very limited field of usefulness. It is specific for certain strains of streptococcus fecalis. It has some value with occasional proteus infections. Dosage of 40,000 to 200,000 units daily parenterally is usually adequate. Allergic reactions to penicillin are being reported in increasing number.

STREPTOMYCIN

Streptomycin, the youngest of the chemotherapeutic family, has proven effective against over 80 percent of the Gram-negative, and also many of the Gram-positive organisms found in the urinary tract. It is of particular value against proteus vulgaris and aerobacter aerogenes, but it is effective against most bacillus coli, some pyocyaneus, and many staphylococci. In many patients sterilization of the urine takes place, but in others a clinical remission is induced without sterilization of the urine. Especially when obstruction is present is permanent sterilization of the urine rare. Furthermore, temporary benefit has been obtained in some patients with tuberculosis. It must be stated, however, that the very promising results of the in vitro experiments have not always been attained in the human subject.

Unlike penicillin, streptomycin is excreted slowly and 40 to 60 percent appears in the urine in 24 hours, against 60 percent in one hour for penicillin. Streptomycin excretion continues for 48 hours after administration ceases. The dosage must usually be high, 2 to 4 gm. per day, administered intravenously or intramuscularly. at 3 to 6 hour intervals. However, recent work has shown some more sensitive organisms, e.g. certain E. coli, to respond well to 1 gm. per day. In vitro strain sensitivity should be tested if possible. The use of sodium bicarbonate or potassium citrate by mouth in conjunction with streptomycin may increase its effectiveness. The drug does not impair renal function.

The disadvantages of streptomycin are the excessive cost, the necessity for injections, and the unpleasant side reactions such as local irritation at the site of injection, headache, vertigo and deafness, and sensitization, with fever and rash. With 3 gm. a day such reactions have been reported to occur in 46 percent and with 4 gm. per day in 60 percent of patients. With the newer, more purified preparations these figures may have to be revised. Anemia and neutropenia plus purpura have been reported. Finally, many organisms very rapidly build up streptomycin resistance. To obviate this, maximum injections must be given from the start. This whole subject is still in its infancy, and many changes may arise in the present conception of the indications and contraindications for the use of streptomycin.

MANDELIC ACID

Mandelic acid is a drug effective in the treatment of many urinary tract infections. While the results are not as dramatic as with some of the newer agents, it is also less toxic and has been unnecessarily neglected. However, it acts only if the urine has been rendered acid at least to pH 5.5 by the addition of ammonium chloride, usually 5 to 8 gm. a day of the enteric coated tablets. The urinary acidity should be tested repeatedly by nitrazene paper. Calcium, sodium or ammonium mandelate in 10 to 14 gm. doses per day after meals is usually adequate, and with the ammonium salt less added acidification may prove necessary. Mandelic acid acts only through its effect on the urine, so that fluids must be limited to 1000 to 1500 cc. which makes it unwise for a patient with a high fever. It is also contraindicated in the presence of elevated blood urea, and it is not tolerated well by old people. Nausea can often be prevented by administration after meals. It is a bacteriocidal against most Gram-negative organisms such as E. coli, aerobacter aerogenes and against some B. pyocyaneus, although the latter bacillus, being a urea splitter, makes the urine hard to acidify. Mandelic acid is also effective against staphylococci, hemolytic streptococci, nonhemolytic streptococci, and against streptococcus fecalis.

METHANAMINE

Methanamine, the oldest of the antiseptics in common usage, still has a field of usefulness. In dosage of 0.6 gm. 3 to 4 times a day in combination with sodium acid phosphate or preferably with ammonium chloride sufficient to acidify the urine to pH 5.5, it will sterilize many B. coli infections, and it is milder and produces less toxic effects. It lends itself particularly to the treatment of low-grade chronic infections, especially in the aged. However, hematuria must be watched for.

PYRIDIUM

Pyridium, one representative of the azo dye group, is not a potent bacteriocidal agent. It has value in

some chronic low-grade infections, especially where acidification is difficult. It seems effective both in alkaline and acid urines.

ARSPHENAMINE

Arsphenamine has been found effective against certain rare cases of abacterial pyuria where tuberculosis has been excluded.

The medical treatment of urinary tract infections, as herein outlined, can be curative. It is important to remember, however, that infection is often present because of stasis or obstruction. There may be obstruction due to stricture, to prostatic hypertrophy, to cystocele, to tumor, or to calculus as well as to many other factors. Permanent sterilization of the urinary tract is difficult in the face of these obstacles. Of greater importance, the overlooking of the other factor may have serious effects for the patient. Obstruction may lead to chronic hydronephrosis, to renal failure, to hypertension, and to death.

No patient whose urine does not promptly become sterile and remain so for several weeks after therapy should be discharged. Every patient with acute pyelonephritis whose urine does not become sterile within one to two weeks under active treatment should have further investigation, including at least intravenous pyelography. Three to four weeks' treatment of the patient with chronic disease should be similarly considered an adequate test of the effectiveness. Suggestion of obstruction should indicate the assistance of a urologist. During the early stages of acute illness, instrumentation and even pyelography are unwise, but the patient who is not responding to conservative measures must be subjected to further study.

SUMMARY

Treatment of pyelonephritis or cystitis should be by the general practitioner or internist.

Effective therapy requires bacteriological diagnosis by smear or culture.

In treatment of acute infections parenteral fluids are often given too fast and without regard for content of salt.

Antibiotics include streptomycin, penicillin, sulfonamides, mandelic acid, methanamine, pyridium, neoarsphenamine.

Sulfonamides, even in small doses, may produce grave reactions, and patients require constant laboratory and clinical supervision. When equally effective, other agents should be preferred to sulfonamides.

If disease is refractive to treatment, and urine does not become and stay sterile, search for obstruction must be made with the aid of the urologist.

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